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EXAMINER
FORMAN, BETTY J

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1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,083	SUNDARARAJAN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8 and 10-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8 and 10-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 October 2007 has been entered.

Status of the Claims

2. This action is in response to papers filed 30 October 2007 in which claims 1, 8, 16, 19 were amended to define the cantilever as having an oxide layer. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 10 August 2007 under obviousness-type double patenting over application 10/254,201 are maintained. The '201 application is now issued as U.S. Patent No. 7,270,952. The previous rejections under obviousness-type double patenting over application 10/705,389 are withdrawn in view of cancellation of the conflicting claims in the '389 application.

The previous rejections under 35 U.S.C. 103(a) are maintained. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Claims 1-2, 5-8, 10-22 are under prosecution.

Claim Interpretation

3. The claims have been amended to define the cantilever as having an oxide layer. The claims define a property of the oxide layer as "to reduce noise and respond proportionally to" a

mass depended property change. However, the properties recited in the claim are not deemed to limit the structural elements of the device.

It is noted that In re Best (195 USPQ 430) and.In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter in which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-2, 5-8 and 10-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baller et al (WO 01/33226, published 10 May 2001) in view of Williams et al (WO 99/57321, published 11 November 1999) and Warthoe (U.S. Patent Application Publication No. 2003/0054344, filed 30 August 2001) or Rothberg et al (U.S. Patent No. 6,274,320, issued 14 August 2001)

Regarding Claim 1, Regarding Claim 1, Baller et al disclose an apparatus for nucleic acid sequencing (page (page 13, lines 24-25).

The apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the

cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), one or more reagent reservoirs in fluid communication with the chamber (i.e. input #112/output #113, Fig. 8), a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and re-use (page 4, lines 15-18).

Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides and do not teach an oxide layer on the cantilever.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and

page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential

addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 2, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 5, Baller et al disclose the apparatus wherein the detection unit comprises a piezoresistor (page 7, lines 15-22).

Regarding Claim 6, Baller et al disclose the apparatus wherein the detection unit comprises a laser (page 7, lines 23-25).

Regarding Claim 7, Baller et al disclose the apparatus wherein the detection unit detects deflection of the cantilever (page 12, lines 12-17).

Regarding Claim 8, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8). Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and

re-use (page 4, lines 15-18). Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for

detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 10, Baller et al disclose the apparatus wherein the data processing and control unit is a computer (PC #111, Fig. 8).

Regarding Claim 11, Baller et al disclose the apparatus wherein the detection unit comprises a laser and a position sensitive photo detector (page 15, line 28-page 16, line 1).

Regarding Claim 12, Baller et al disclose the apparatus wherein the detection unit comprises a piezoresistor (page 7, lines 15-22).

Regarding Claim 13, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 14, Baller et al disclose the apparatus further comprising an array of cantilevers (#102) wherein each cantilever is "associated with the same molecule".

The claims are given the broadest reasonable interpretation consistent with the broad claim language and specification wherein "associated with" is not defined. The apparatus of Baller has an array of cantilevers within a liquid cell having an inlet for fluid flow into the cell. The cell is used e.g. hybridization. Any molecule (e.g. buffer molecules) put into the cell via the inlet would be "associated with" each cantilever as claimed.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Regarding Claim 15, Baller et al disclose the apparatus further comprising an array of cantilevers (#102) wherein each cantilever is "associated with a different molecule" i.e. have different affinities for a target (page 8, lines 24-27; page 11, lines 14-20; and page 12, lines 18-23).

Regarding Claim 16, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) each comprising one or more covalently attached nucleic acid templates (thiol modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20), a piezoresistor embedded at the fixed end of the cantilever (page 7, lines 15-22), a detection unit "operably coupled" to the piezoresistor to detect deflection (page 7, lines 15-22) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al further teach that detection of support-immobilized molecules using AMF have numerous disadvantages e.g. results are difficult to reproduce, strong dependence on and sensitivity to environmental parameters (page 1, lines 18-22) Baller et al further teach that

cantilever-immobilized molecules do not suffer the same disadvantages due to the advantages provided by the cantilever e.g. reliable recognition of molecules and reliable detection of properties in various environments (page 1, lines 23-26) thereby providing a very sensitive system with fast responses, suitable for mass production and re-use (page 4, lines 15-18).

Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 17, Baller et al disclose the apparatus further comprising a resistance measuring device (page 7, line 18).

Regarding Claim 18, Baller et al disclose the apparatus wherein the nucleic acids are about 10 nucleotides in length (e.g. 12 and 16 mer, page 12, lines 18-23).

Regarding Claim 19, Baller et al disclose an apparatus comprising a analysis chamber (Fig. 8) containing one or more cantilevers (#102) coated with a substance (e.g. gold layer, page 13, lines 13-15) each comprising one or more covalently attached nucleic acid templates (thiol

modified DNA attached to gold-coated cantilever, page 13, lines 9-15) wherein the cantilevers are responsive to deflection produced by changes in mass (i.e. addition of complementary sequence adds mass to the cantilever and causes deflection, page 13, lines 1-20) a detection unit operably coupled to the cantilever (PSD, #108) and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit (PC #111, Fig. 8).

Baller et al disclose the apparatus wherein the cantilevers function to detect biomolecule binding (page 9, lines 22-24) and are useful for determining base sequence analysis (page 13, lines 22-25) but they are silent regarding addition of polymerase to the analysis chamber. Baller et al do not teach the device wherein having a reservoir with a polymerase or multiple reservoirs for sequential addition of nucleotides.

However, these elements were well known and routinely practiced in the art at the time the claimed invention was made as taught by Williams, Warthoe and Rothberg.

First, Williams teaches a similar device for nucleic acid sequencing (Abstract). The device comprising an analysis chamber comprising one or more double stranded nucleic acids (primer/template hybrid) wherein the nucleic acids are covalently attached to a support (page 11, lines 22-29) wherein the chamber is responsive to the addition of sequentially added and labeled nucleotides (page 19, lines 3-13), the apparatus further comprising one or more reagent reservoirs in fluid communication with the chamber, a detection unit operably coupled to the chamber and a data processing and control unit "operably coupled" to the chamber, reservoirs and detection unit and further comprising a polymerase within the chamber (Claims 27-42 and page 7, lines 6-13 and pages 8-11) and further teach the detection device having a sensitivity for detection of nucleotide incorporation (i.e. AFM, page 22, line 30-page 23, line 16)

Second, Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports

for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

Finally, Rothberg teaches a similar device for sequencing (Abstract). The apparatus comprising an analysis chamber having immobilized nucleic acids and polymerase and reservoirs configured for sequential addition of mass labeled-nucleotides (Column 18, line 40-Column 19, line 35) and a data processing and control unit operably coupled to the device for detection and analysis of nucleotide addition (Column 30, lines 34-55). It is noted that the instant specification (¶ 74-76) broadly defines mass labeled nucleotides so as to encompass the labels of Rothberg.

Hence, all the structural elements of the claims were well known and routinely practiced in the art of nucleic acid sequencing.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made combine the teaching of Williams, Warthoe and Rothberg with that of Baller. Both Williams and Warthoe teach the cantilevered device comprising a polymerase and addition of labeled nucleotides and both clearly suggest a plurality of reservoirs for the nucleotides. And multiple reservoirs for sequential addition of nucleotides was also well known as taught by Rothberg. One of ordinary skill in the art would have been motivated to combine the teaches to provide the device of Baller with multiple reservoirs configured for sequential addition of nucleotides for the expected benefit of providing an integrated device as desired in the art (Warthoe, ¶ 2) and optimizing the controlled addition of reagents as provided by the sequential addition of reagents as taught by Rothberg (Column 19, lines 29-35).

Regarding Claim 20-21, Baller et al disclose the substance is an alloy e.g. gold (page 13, lines 9-15).

Regarding Claim 22, Baller disclose the apparatus wherein the nucleic acids are coupled to the cantilever through a thiol group (page 13, lines 9-15).

Response to Arguments

6. Applicant asserts that the cited references do not teach an oxide layer on the cantilever. However, as cited above, Warthoe et al teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of Baller so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

NEW GROUNDS FOR REJECTION NECESSITATED BY THE IDS OF 10/31/2007

7. Claims 1-2, 5, 7-8, 10, 12-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furcht et al (U.S. Patent No. 6,054,277, issued 25 April 2000) in view of Warthoe (U.S. Patent Application Publication No. 2003/0054344, filed 30 August 2001)

Regarding Claim 1, Furcht et al teach a device for sequencing (Column 4, lines 15-57). The apparatus comprising one or more cantilevers (Fig. 1, #13, Fig. 8a, #88) having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (Column 11, lines 10-64) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (Column 4, lines 37-57) a detection unit coupled to the cantilever (Column 11, lines 45-63) and a data processing and control unit coupled to the chamber (Column 6, lines 42-55, Column 8, lines 7-20) and further comprises polymerase and labeled nucleotides (Column 11, lines 10-64). Furcht et al does not teach an oxide layer on the cantilever. However, this element was well known in the art at the time the claimed invention was made as taught by Warthoe.

Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of Furcht et al so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

Regarding Claim 2, Furcht et al is silent regarding the length of the template however, Warthoe teaches the similar device wherein the template has the claimed length (e.g. ¶ 198).

Regarding Claim 5, Furcht et al disclose the detection device comprises a piezoelectric detector (Column 11, lines 30-62).

Regarding Claim 7, Furcht et al disclose the detection unit detects mass change of the cantilever structure (Column 11, lines 30-62).

Regarding Claim 9, Furcht et al teach a device for sequencing (Column 4, lines 15-57). The apparatus comprising one or more cantilevers (Fig. 1, #13, Fig. 8a, #88) having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (Column 11, lines 10-64) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (Column 4, lines 37-57) a detection unit coupled to the cantilever (Column 11, lines 45-63) and a data processing and control unit coupled to the chamber (Column 6, lines 42-55, Column 8, lines 7-20) and further comprises polymerase and labeled nucleotides (Column 11, lines 10-

64). Furcht et al does not teach an oxide layer on the cantilever. However, this element was well known in the art at the time the claimed invention was made as taught by Warthoe.

Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of Furcht et al so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

Regarding Claim 10, Furcht et al teach the device comprises a computer (column 8, lines 20-23).

Regarding Claim 12, Furcht et al disclose the detection device comprises a piezoelectric detector (Column 11, lines 30-62).

Regarding Claim 13, Furcht et al is silent regarding the length of the template however, Warthoe teaches the similar device wherein the template has the claimed length (e.g. ¶ 198).

Regarding Claim 14, Furcht et al disclose the apparatus further comprising an array of cantilevers wherein each cantilever is "associated with the same molecule".

The claims are given the broadest reasonable interpretation consistent with the broad claim language and specification wherein "associated with" is not defined. The apparatus of Furcht has an array of cantilevers within a liquid cell having an inlet for fluid flow into the cell. The cell is used e.g. hybridization. Any molecule (e.g. buffer molecules) put into the cell via the inlet would be "associated with" each cantilever as claimed.

Regarding Claim 15, Furcht et al disclose the apparatus further comprising an array of cantilevers wherein each cantilever is "associated with a different molecule" (Column 11, lines 2-10).

Regarding Claim 16, Furcht et al teach a device for sequencing (Column 4, lines 15-57). The apparatus comprising one or more cantilevers (Fig. 1, #13, Fig. 8a, #88) having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (Column 11, lines 10-64) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (Column 4, lines 37-57) a detection unit coupled to the cantilever (Column 11, lines 45-63) and a data processing and control unit coupled to the chamber (Column 6, lines 42-55, Column 8, lines 7-20) and further comprises polymerase and labeled nucleotides (Column 11, lines 10-64) wherein the detection device comprises a piezoelectric detector (Column 11, lines 30-62).

Furcht et al does not teach an oxide layer on the cantilever. However, this element was well known in the art at the time the claimed invention was made as taught by Warthoe.

Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of Furcht et al so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

Regarding Claim 17, Furcht et al teach the detection device comprises a resistance measuring device (Column 10, lines 16-27).

Regarding Claim 18, Furcht et al is silent regarding the length of the template however, Warthoe teaches the similar device wherein the template has the claimed length (e.g. ¶ 198).

Regarding Claim 19, Furcht et al teach a device for sequencing (Column 4, lines 15-57). The apparatus comprising one or more cantilevers (Fig. 1, #13, Fig. 8a, #88) having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (Column 11, lines 10-64) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (Column 4, lines 37-57) a detection unit coupled to the cantilever (Column 11, lines 45-63) and a data processing and control unit coupled to the chamber (Column 6, lines 42-55, Column 8, lines 7-20) and further comprises polymerase and labeled nucleotides (Column 11, lines 10-64) wherein the detection device comprises a piezoelectric detector (Column 11, lines 30-62).

Furcht et al does not teach an oxide layer on the cantilever. However, this element was well known in the art at the time the claimed invention was made as taught by Warthoe.

Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182) and selected pattern of immobilized DNA (¶ 35, Fig. 6).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of Furcht et al so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

Regarding Claims 20-22, Furcht et al disclose the cantilever is comprises gold (Column 11, lines 14-17). And Warthoe et al disclose the similar device wherein the cantilever comprises gold for immobilization of thiol-modified DNA (¶ 35, Fig. 6).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims1-2, 5-8, 10-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 7,270,952 in view of in view of Lindsay et al (U.S. Patent No. 5,750,989).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an apparatus comprising cantilever structures, detection unit and data processing/control unit. The claim sets merely differ in

that the instant claims define the cantilever as part of an analysis chamber. While the patent claims do not require a chamber, cantilevers chambers were well known and routinely practiced in the art at the time the claimed invention was made as taught by Lindsay et al who teach that the chamber permits sample analysis within a controlled environment (Column 4, lines 12-34). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the chamber of Lindsay et al to the '083 apparatus for the expected benefit of environmentally controlled sample analysis as desired in the art (Lindsay et al, Column 4, lines 12-34). The claim sets further differ in that the '201 claims require a dielectric sphere, laser and objective lens. However, the instant claim language "comprising" encompasses the additional elements recited in the '201 claims. For these reasons, the claim sets are not patentably distinct.

Response to Arguments

10. Applicant has provided no arguments regarding the above rejection. The rejection is maintained. This rejection is no longer provisional because the conflicting claims are patented.

11. Claims 1-2, 5-8, 10-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-22 of copending Application No. 11/445,884 in view of Warthoe (U.S. Patent Application Publication No. 2003/0054344, filed 30 August 2001).

. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to almost identical apparatus comprising cantilever structures, detection unit and data processing/control unit. The claim sets merely differ in that the instant claims define the cantilever as having an oxide layer. However, cantilevers with an oxide layer were well known as taught by Warthoe.

Warthoe teaches a similar device for sequencing (¶ 43). The apparatus comprising one or more cantilevers having a partially double stranded nucleic acid attached wherein the cantilevers detect mass change resulting from nucleotide addition/primer extension (¶ 43) and further teach the device comprises reagent reservoirs, channels and ports for selective addition to the device (¶ 128-129) and further comprises polymerase and labeled nucleotides (Example 2) thereby providing an inexpensive and integrated device for routine target detection as desired in the art (¶ 2 and 15). Warthoe et al further teach the cantilever having an oxide layer so as to electronically isolate the cantilever (¶ 182) and selected pattern of immobilized DNA (¶ 35, Fig. 6).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the oxide of Warthoe to the cantilever of '844 so as to provide electronic isolation as desired in the cantilever art (Warthoe, ¶ 182).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions

daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BJ Forman, Ph.D.
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Art Unit: 1634
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